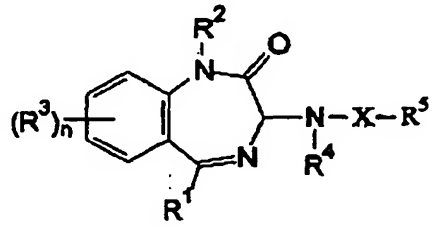
CLAIMS

1. Use of a compound which is (a) a benzodiazepine derivative of the formula (I) or an N-oxide thereof or (b) a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in treating or preventing an RSV infection



(I)

wherein:

- R^1 represents C_{1-6} alkyl, aryl or heteroaryl;
- R^2 represents hydrogen or C_{1-6} alkyl;
- each R^3 is the same or different and represents halogen, hydroxy, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylthio, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, amino, mono(C_{1-6} alkyl)amino, di(C_{1-6} alkyl)amino, nitro, cyano, $-CO_2R'$, $-CONR'R''$, $-NH-CO-R'$, $-S(O)R'$, $-S(O)_2R'$, $-NH-S(O)_2R'$, $-S(O)NR'R''$ or $-S(O)_2NR'R''$, wherein each R' and R'' is the same or different and represents hydrogen or C_{1-6} alkyl;
- n is from 0 to 3;
- R^4 represents hydrogen or C_{1-6} alkyl;
- X represents -CO-, $-CO-NR'-$, -S(O)- or $-S(O)_2-$, wherein R' is hydrogen or a C_1-C_6 alkyl group; and
- R^5 represents an aryl, heteroaryl or heterocyclyl group, which group is substituted by a C_1-C_6 hydroxyalkyl group or a $-(C_1$-C_4 alkyl)-X_1-(C_1-C_4 alkyl)-X_2-(C_1-C_4 alkyl) group, wherein X_1 represents -O-, -S- or $-NR'-$, wherein R' represents H or a C_1-C_4 alkyl group and X_2 represents -CO-, -SO- or $-SO_2-$, or R_5 represents $-A_1$-Y-A_2, wherein:
- A_1 is an aryl, heteroaryl, carbocyclyl or heterocyclyl group;
- Y represents a direct bond or a C_1-C_4 alkylene, $-SO_2-$, -CO-, -O-, -S- or $-NR'-$ moiety, wherein R' is a C_1-C_6 alkyl group; and

- A_2 is an aryl, heteroaryl, carbocyclyl or heterocyclyl group.

2. Use according to claim 1, wherein R^1 is C_{1-2} alkyl or phenyl.

3. Use according to claim 1 or 2, wherein R^2 is hydrogen.

4. Use according to any one of the preceding claims wherein R^3 is halogen, hydroxy, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} alkylthio, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, amino, mono(C_{1-4} alkyl)amino or di(C_{1-4} alkyl)amino.

5. Use according to claim 4, wherein R^3 is fluorine, chlorine, bromine, C_{1-2} alkyl, C_{1-2} alkoxy, C_{1-2} alkylthio, C_{1-2} haloalkyl, C_{1-2} haloalkoxy, amino, mono(C_{1-2} alkyl)amino or di (C_{1-2} alkyl)amino.

6. Use according to any one of the preceding claims wherein R^4 is hydrogen or C_{1-2} alkyl.

7. Use according to any one of the preceding claims wherein X is -CO- or -CO-NR′- wherein R′ represents hydrogen or a C_1-C_2 alkyl group.

8. Use according to any one of the preceding claims, wherein R^5 is a 5- or 6-membered heterocyclyl or heteroaryl ring which is substituted by a C_1-C_6 hydroxyalkyl group or a -(C_1-C_4 alkyl)-X_1-(C_1-C_4 alkyl)-X_2-(C_1-C_4 alkyl) group, wherein X_1 and X_2 are as defined in claim 1.

9. Use according to claim 8, wherein R^5 is a 5- or 6- membered heteroaryl group which is substituted by a -CH_2-OH or -(C_1-C_4 alkyl)-NR′-(C_1-C_4 alkyl)-S(O)$_2$-(C_1-C_4 alkyl) substituent, wherein R′ is hydrogen or C_1-C_2 alkyl.

10. Use according to any one of the preceding claims, wherein A_1 is an aryl or heteroaryl group.

11. Use according to claim 10, wherein A_1 is a phenyl group, a monocyclic 5- or 6- membered heteroaryl group or a 5- to 6- membered heteroaryl group fused to a monocyclic oxo-substituted 5- to 6- membered heterocyclyl group.

12. Use according to any one of the preceding claims wherein A_1 is unsubstituted or substituted by 1 or 2 substituents selected from halogen, cyano, nitro, C_1-C_4 alkyl, C_1-C_4 haloalkyl and C_1-C_4 alkoxy substituents.

13. Use according to any one of the preceding claims, wherein Y represents a direct bond, a C_1-C_2 alkylene group, $-SO_2-$ or -O-.

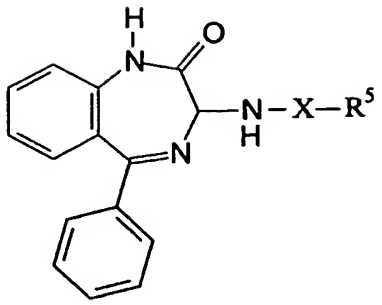
14. Use according to any one of the preceding claims, wherein A_2 is a phenyl, 5- to 6- membered heteroaryl, 5- to 6- membered heterocyclyl or C_3-C_6 cycloalkyl group.

15. Use according to any one of the preceding claims, wherein when A_2 is a heterocyclyl group it is attached to the moiety Y via a N atom.

16. Use according to any one of the preceding claims, wherein A_2 is unsubstituted or is substituted by 1 or 2 substituents which are selected from C_1-C_4 alkyl and halogen substituents when A_2 is a heteroaryl or aryl group and which are selected from C_1-C_4 alkyl, halogen and oxo substituents when A_2 is a carbocyclic or heterocyclyl group.

17. Use according to any one of the preceding claims, wherein A_2 is a piperazinyl, pyridyl, morpholinyl, pyrrolidinyl, piperidinyl, pyrazinyl, cyclopropyl, phenyl or S,S-dioxo-thiomorpholino group, which is unsubstituted or substituted by a C_1-C_2 alkyl group.

18. Use according to any one of the preceding claims wherein the benzodiazepine derivative of formula (I) is a benzodiazepine derivative of formula (Ia):



(Ia)

wherein:

- X is -CO- or -CO-NH- ; and
- R^5 is a 5- to 6- membered heteroaryl group, for example a furanyl group, which is substituted by $-CH_2-OH$ or $-(C_1-C_4$ alkyl$)-N(CH_3)-(C_1-C_4$ alkyl$)-SO_2-(C_1-C_4$ alkyl) or R_5 represents $-A_1-Y-A_2$, wherein:
- A_1 is a phenyl, pyridyl, furanyl, thiazolyl, oxazolyl, isoxazolyl, thienyl or 1H-imidazo[4,5-b]pyridin-2-(3H)-one moiety, which is unsubstituted or substituted by 1 or 2 substituents selected from halogen, cyano, C_1-C_2 alkyl, C_1-C_2 haloalkyl and C_1-C_2 alkoxy substituents;
- Y is a direct bond, a C_1-C_2 alkylene group, $-SO_2-$ or -O-; and
- A_2 is a piperazinyl, pyridyl, morpholinyl, pyrrolidinyl, piperidinyl, pyrazinyl, cyclopropyl, phenyl or S,S-dioxo-thiomorpholino group, which is unsubstituted or substituted by a C_1-C_2 alkyl group.

19. Use according to any one of the preceding claims, wherein the medicament is for use in treating a patient who is a child under two years of age, an adult suffering from asthma, chronic obstructive pulmonary disorder (COPD) or immunodeficiency, an elderly person or a person in a long term care facility.

20. Use according to claim 19 wherein said child suffers from chronic lung disease.

21. Use according to any one of claims 1 to 18 wherein the medicament is for use in preventing RSV infection in an infant less than six years of age who was born after 32 weeks of gestation or less.

22. Use according to any one of the preceding claims, wherein the medicament is suitable for intranasal or intrabronchial administration.

23. Use according to any one of the preceding claims, wherein the medicament further comprises an anti-inflammatory compound or an anti-influenza compound.

24. Use according to claim 23 wherein the anti-inflammatory compound is budesonide or fluticasone.

25. Use according to claim 23 wherein the anti-inflammatory compound is a leukotriene antagonist, phosphodiesterase 4 inhibitor or TNF alpha inhibitor.

26. Use according to claim 23 wherein the anti-inflammatory compound is an interleukin 8 or interleukin 9 inhibitor.

27. Use according to any one of claims 1 to 22 wherein the medicament is coadministered with an anti-inflammatory compound, as defined in any one of claims 24 to 26, or an anti-influenza compound.

28 A method of treating a patient suffering from or susceptible to an RSV infection, which method comprises administering to said patient an effective amount of a compound as defined in any one of claims 1 to 18.

29. A method according to claim 28, wherein said patient is a patient as defined in any one of claims 19 to 21.

30. A method according to claim 28 or 329, wherein said compound is administered intranasally or intrabronchially.

31. An inhaler or nebuliser containing a medicament which comprises

(a) a compound as defined in any one of claims 1 to 18, and

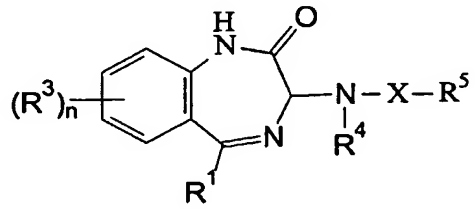
(b) a pharmaceutically acceptable carrier or diluent.

32. A product comprising a compound as defined in any one of claims 1 to 18 and an anti-inflammatory compound, as defined in any one of claims 24 to 26, or an anti-influenza compound.

33. Use of a product accoding to claim 32 in the manufacture of a medicament for use in the treatment of concomitant RSV and influenza infections.

34. Use of a compound as defined in any one of claims 1 to 18 in the manufacture of a medicament for use in the treatment of human metapneumovirus, measles, parainfluenza viruses, mumps, yellow fever virus (B5 strain), Dengue 2 virus or West Nile virus.

35. A compound which is (a) a benzodiazepine derivative of formula (Ib) or an N-oxide thereof, or (b) a pharmaceutically acceptable salt thereof



(Ib)

wherein R_1, R_3, n, R_4, X and R_5 are as defined in any one of claims 1 to 18.

36. A compound according to claim 35, wherein R_1 is an unsubstituted phenyl group.

37. A compound according to claim 35 or 36, wherein when A_1 is a heteroaryl group, it is other than a 5-methyl-isoxazolyl moiety.

38. A compound according to any one of claims 35 to 37, wherein A_1 is an aryl or heteroaryl moiety.

39. A compound according to any one of claims 35 to 38, wherein X is -CO- or -CO-NR′-, wherein R′ is as defined in any one of claims 1 to 18, provided that when X is -CO-NR′-, the moiety -A_1-Y-A_2 is -phenyl-O-phenyl.

40. A compound according to any one of claims 35 to 39, wherein A_2 is other than a 4- to 10- membered saturated cycloalkyl ring, in which one of the carbon atoms is replaced by a N atom.

41. A compound according to any one of claims 35 to 40, wherein A_2 is a piperazinyl, pyridyl, pyrrolidinyl, pyrazinyl, cyclopropyl, phenyl or S,S-dioxo-thiomorpholino group which is unsubstituted or is substituted by a C_1-C_2 alkyl group.

42. A compound according to claim 35, wherein the benzodiazepine derivative of the formula (Ib) is:

6-(4-Methyl-piperazin-1-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4] diazepin-3-yl)-nicotinamide;

3,4,5,6-Tetrahydro-2H-[1,2']bipyridinyl-5'-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;

(S)-2-(1,1-Dioxo-1λ6-thiomorpholin-4-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl-benzamide;

(S)-2-Chloro-4-morpholin-4-yl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4] diazepin-3-yl)-benzamide;

(S)-2-(1,1-Dioxo-1λ6-thiomorpholin-4-yl)-4-fluoro-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl-benzamide;

(S)-5-Chloro-2-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;

(S)-2-(1,1-Dioxo-1λ6-thiomorpholin-4-yl)-5-fluoro-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;

(S)-5-(4-Methyl-piperazin-1-ylmethyl)-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;

(S)-5-Pyrrolidin-1-ylmethyl-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-

1H-benzo[e][1,4]diazepin-3-yl)-amide;
(S)-5-Piperidin-1-ylmethyl-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;
(S)-5-Dimethylaminomethyl-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;
(S)-4-Fluoro-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-2-piperidin-1-yl-benzamide;
(S)-4-Fluoro-2-morpholino-4-yl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;
(S)-4-Cyano-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-2-pyrrolidin-1-yl-benzamide;
(S)-4-Cyano-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-piperidine-1-yl-benzamide;
(S)-N-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-2-pyrrolidin-1-yl-4-trifluoromethyl-benzamide;
(S)-N-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-2-piperidin-1-yl-4-trifluoromethyl-benzamide;
(S)-2-Morpholin-4-yl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-4-trifluoromethyl-benzamide;
(S)-N-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-2-pyrrolidin-1-yl-5-trifluoromethyl-benzamide;
(S)-2-Morpholin-4-yl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-5-trifluoromethyl-benzamide;
(S)-2-Morpholin-4-yl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-nicotinamide;
(S)-2-(1,1-Dioxo-1λ6-thiomorpholin-4-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-nicotinamide;
(S)-2-(1,1-Dioxo-1λ6-thiomorpholin-4-yl)-3-methyl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;
(S)-2-(1,1-Dioxo-1λ6-thiomorpholin-4-yl)-4-methyl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;
(S)-2-(1,1-Dioxo-1λ6-thiomorpholin-4-yl)-6-methyl-N-(2-oxo-5-phenyl-2,3-

dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;

(S)-2-Chloro-6-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;

(S)-3-Cyclopropyl-2-oxo-2,3-dihydro-imidazo[4,5-b]pyridine-1-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;

(S)-3-(4-Methyl-piperazine-1-sulfonyl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;

(S)-4-(4-Methyl-piperazin-1-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4] diazepin-3-yl)-benzamide;

(S)-N-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-3-(piperidine-1-sulfonyl)-benzamide;

(S)-3-(Morpholine-4-sulfonyl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4] diazepin-3-yl)-benzamide;

(S)-5-Morpholin-4-ylmethyl-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;

(S)-5-Hydroxymethyl-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;

(S)-5-(1,1-Dioxo-1λ6-thiomorpholin-4-ylmethyl)-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;

(S)-2-Chloro-4-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;

(S)-2-Chloro-5-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;

(S)-5-{[(2-Methanesulfonyl-ethyl)-methyl-amino]-methyl}-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl-amide;

(S)-2-Pyridin-3-yl-thiazole-4-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;

(S)-2-Pyridin-4-yl-thiazole-4-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;

(S)-4-Methyl-2-pyrazin-2-yl-thiazole-5-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;

(S)-2-Morpholin-4-ylmethyl-furan-3-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-

1H-benzo[e][1,4]diazepin-3-yl)-amide;
(S)-3-Morpholin-4-ylmethyl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4] diazepin-3-yl)-benzamide;
(S)-5-Morpholin-4-ylmethyl-isoxazole-3-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;
(S)-3-Morpholin-4-ylmethyl-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;
(S)-5-Pyridin-2-yl-thiophene-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;
(S)-2-Methyl-4-(morpholin-4-sulfonyl)-furan-3-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;
(S)-6-Morpholin-4-yl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-nicotinamide;
(S)-3-Morpholin-4-ylmethyl-thiophene-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;
(S)-5-Morpholin-4-ylmethyl-thiophene-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;
2-Morpholin-4-yl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;
(S)-5-Phenyl-oxazole-4-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide; or
1-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-3-(4-phenoxy-phenyl)-urea.

43. A compound according to any one of claims 35 to 42 for use in a method of treating the human or animal body.

44. A pharmaceutical composition comprising a compound according to any one of claims 35 to 43, and a pharmaceutically acceptable diluant or carrier.

45. A composition according to claim 44 comprising an optically active isomer of a compound according to any one of claims 35 to 42.

46. A composition according to claim 44 or 45 which is in the form of a tablet, troche, lozenge, aqueous or oily suspension, dispersible powders or granules.